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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,445	08/24/2006	Michael E. Jung	58086-235854 (2004-129-2)	6734

26694 7590 07/23/2008

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EXAMINER	
RAO, SAVITHA M	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
07/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,445	JUNG ET AL.	
	Examiner	Art Unit	
	SAVITHA RAO	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *3-6 and 11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 7-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/24/2006 and 11/01/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1- 14 are pending and are subject of this office action. Claims 3-6, 11-14 are withdrawn from consideration as being drawn to non elected invention.

Claims 1-2 and 7-10 are under consideration in the instant office action

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statement filed 11/01/2007 and 08/24/2006. The Examiner has considered the reference cited therein to the extent that each is a proper citation. Please see the attached USPTO Form 1449.

The foreign documents cited on 1449 dated 11/01/2007 have been lined out since the documents were not in English and English translations were not provided. The "International search report " on 1449 dated 08/24/2006 and 11/01/2007 have been lined out because it is not a published document and therefore cannot have a date of publication which is required for a citation in the non-patent document area of 1449. NPL references C3 and C9 on 1449 dated 11/01/2007 have been lined out due to lack of date of publication.

Election/Restrictions

Applicant's election with traverse of Group 1 (claims 1-2 and 7-10) in the reply filed on 07/07/08 is acknowledged. The traversal is on the ground(s) that the reference used by the examiner to demonstrate lack of unity Claussner '509 did not disclose the compound as claimed where in the R3 substituent is an azide.

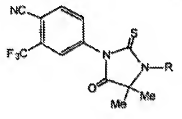
Examiner finds the applicant's argument persuasive. Even without using the reference to break the unity, the groups possesses lack of unity for the following reasons

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1-2, 7-10 to a composition of matter comprising a compound having the formula



wherein R is $(CH_2)_nN_3$ or $N_3C_6H_4$ and where n is from 3 to 8.

Group II, claims 3-6 are drawn to a method of inhibiting prostate specific antigen production in prostate cancer cell, inhibiting growth of a human prostate cancer cell, antagonizing the function of the ligand binding domain of the androgen receptor polypeptide in a prostate cancer cell upon contacting the cell with a sufficient amount of the compound claimed in Group I.

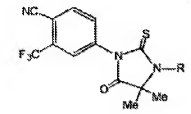
Group III, claims 11-14 drawn to a method of making a composition of matter comprising compound claimed in Group I.

An international application should relate to only one invention or, if there is more than one invention, the inclusion of those inventions in one international application is only permitted if all inventions are so linked as to form a single general inventive concept (PCT Rule 13.1). With respect to a group of inventions claimed in an international application, unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features. The claims herein lack unity of invention under PCT rule 13.1 and 13.2 since, under 37 CFR 1.475(a).

Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

Groups I and III lack unity of invention under 37 CFR 1.475 since the three groups (I-III) are not unified by the same or corresponding special feature as detailed below.

The special technical feature in Group I is the composition of the compound of



wherein R is $(CH_2)_nN_3$ or $N_3C_6H_4$ and where n is from 3 to 8.

The special technical feature in Group II is the actual step of contacting the mammalian prostate cancer cell with the compound of group 1, resulting in inhibition of production of prostate specific antigen production, or inhibition of growth of human prostate cancer cell or antagonizing of the androgen receptor.

The special technical feature in Group III which is the method for making a composition of matter comprising the compound involves, identification of the raw materials or individual components needed to make the final product and the actual process of combining the raw materials to obtain the final product.

Accordingly there is no same or corresponding special technical features unifying Groups I-III and thereby they lack unity.

Furthermore for Groups I –III, under 37 CFR 1.475(b) a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations:

(1) A product and a process specially adapted for the manufacture of said product; or

(2) A product and a process of use of said product; or

(3) A product, a process specially adapted for the manufacture of said product, and a use of said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of said product, and an apparatus or means specifically designed for carrying out the said process.

And according to 37 CFR 1.475(c): if an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b), unity of invention might not be present.

Therefore, since in the instant application the claims are drawn to three distinct inventions, based on, composition and two different methods of using the compositions as shown above, and according to 37 CFR 1.475(e): the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claims. The claims, therefore, lack unity of invention.

Accordingly, claim 3-6, 11-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 07/08/2008.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

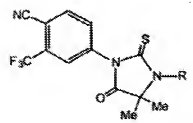
invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1, 2 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sovak et al (US 5656651, referenced in the IDS) in view of Chu et al. (US 6949521)

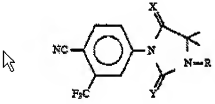
Instant claims 1, 2, 7-10 are drawn towards a composition of matter comprising a compound having the formula and a pharmaceutically acceptable carrier.



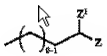
wherein R is $(CH_2)_nN_3$ or $N_3C_6H_4$ and where n is from 3 to 8.

Sovak teaches substituted phenylthiohydantoins for use in detecting the presence of tumor cells having androgenic receptors and providing for cytostatic and cytotoxic activity toward such cells (abstract). Sovak teaches N-substituted arylthio-4',

4'-dimethylhydantoins and that the compound finds uses in diagnosis and/or therapy associated with androgenic receptors and that the subject compounds have high affinity for androgen receptors of a variety of cell types and are able to exert at least one of proliferation inhibition or cytotoxicity for thereby or preferential binding for use as a detecting medium for cells and tissues comprising androgen receptors or for other identification. (col.2, lines 25-36). Sovak teaches that tissue comprising cells with androgen receptors include prostate tissue, ovary tissue testes etc (col.3, lines 4-6). Sovak teaches compounds having the following formula



Wherein X is oxygen or nitrogen, with the proviso that when R is iodoaryl, X may be sulfur; Y is sulphur, with the proviso that when R is iodoaryl group, Y may be sulphur, oxygen or nitrogen, preferably X and Y are different; R is an organic group, which may be aliphatic, alicyclic, aromatic, heterocyclic, or combinations thereof as defined below. The first group of compounds will comprise monothiohydantoins, where the other oxo group of the hydantoin will be oxygen or nitrogen. These groups will, for the most part, have R having the following formula



Wherein: Z is hydroxyl, amino, a substituted amino or a 4-diazolyl, particularly a 4-(1',3'-imidazolyl); Z^1 is hydrogen, hydroxyl, or may be taken together with Z to provide for olefinic or acetylenic unsaturation, or a 2,2-dimethyldioxalane. (col.3, lines 7-41)

Sovak teaches that the the substituents on amino nitrogen may be varied widely, depending upon the use of the compound. For cytotoxicity or antiproliferative activity, the amino group may be unsubstituted or substituted, particularly with the single acyl group, where the acyl group may serve to enhance the activity of the compound by changing its pharmacokinetic activities, by providing for a second cytotoxic or antiproliferative compound, by providing for a chelating agent for chelating a metal ion, particularly a radioactive metal or non-metallic on, for carrying a radioopaque atom, or the like. Radioactive elements include fluorine, iodine, gadolinium, technetium, etc (col.3, lines 42-53). Sovak further teaches that various cytotoxic agents such as methotrexate, taxol, adriamycin etc. may be employed which are joined to the subject hydantoins by any convenient linking groups which does not significantly diminish the cytotoxic or antiproliferative activity of the compound (col.4, lines 27-32). Sovak teaches that the subject compositions may be formulated in accordance with conventional ways for use in vivo. The subject compounds are found to be stable in human plasma at physiological temperatures. The subject compounds are found to have substantially greater cytostatic and cytotoxic effects in inhibiting cell growth for neoplastic cells, as compared to normal cells, i.e. having a high therapeutic index. The subject compositions are readily formulated in conventional carriers, such as saline, phosphate buffered saline, vegetable oils, ethanol, or other physiologically acceptable carrier

(col.5, lines 7-17). Accordingly Sovak provides one of ordinary skill in the art motivation to develop composition comprising phenylthiohydantoin derivatives.

What Sovak does not teach is the specific compound claimed in instant application wherein the N substitution is either a $(CH_2)_n N_3$ n=3-8 or $C_6H_4 N_3$.

This deficiency is cured by the teachings of Chu et al

Chu et al teaches prodrug compositions comprising azide derivatives of drugs which are capable of being converted to the drug in vivo. (abstract) Among the preferred class of azide derivative Chu teaches those of nucleoside analogs , azide derivatives of aminoglycoside antibiotics which are primary amines, ketones, or hydroxy-substituted compounds, Azide derivatives of sulfonamides which are primary amines or ketones and azide derivatives of biologically active acyclic amines, ketones and hydroxy-substituted compounds, including arylalkyl, heterocyclic arylalky, and cyclic aliphatic compounds where the amine or oxygen moiety is on the ring (col.1, lines 1-65)). Chu additionally teaches that the corresponding azides may be formed for drugs useful for virtually any therapeutic purposes, so as to increase the half-lives of said drugs and suitable drugs can be identified by those skilled in the art form those having amine, carbonyl or hydroxy substituents. Additionally, Chu teaches that formulation of corresponding azides may be readily accomplished by those of ordinary skill in the art without undue experimentation by means known in the art (col. 12, lines 28-46). Accordingly Chu provides one or ordinary skill in the art motivation to derivatize a known drug with an azide functionality to extend the half-life of that particular drug.

Regarding the properties recited in claims 7-8 (wherein the compound inhibits the growth of hormone refractory prostate cancer cells, wherein the compound has been previously subjected to a method of examining the physiological effect etc.), a composition and its properties cannot be separated. The composition and the compound are understood to carry the characteristics associated with them. The prior art does not measure the properties recited in the instant claims 7 and 8, however, because the prior art compositions has the similar components as required by applicant's claims, it necessarily must exhibit and have the same properties. Thus the properties of instant claim 7-8 are inherent to the prior art compositions. Office lacks laboratory facilities to test the prior art compositions. It is incumbent upon applicants to provide data demonstrating that the properties of the disclosed prior art compositions are different from the claimed compositions. Thus, because the prior art compositions are the same as claimed by applicants, the recited properties are inherent to the prior art compositions

The differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. The primary reference teaches structurally related compounds to those claimed in the instant application which possess cytotoxic effects and the secondary reference of Chu teaches that modification of the amine group in any known therapeutics to azide group increases the bioavailability and half-life of the known therapeutic thereby increasing its efficacy. Accordingly, It would have been *prima facie*

obvious to the skilled artisan to combine the teachings of Sovak and Chu to synthesize the instantly claimed compound. An ordinarily skilled artisan would have been motivated to use the dimethylphenyl hydantoin, N-substituted with amine moiety taught by Sovak and modify the amine function to azide functionality as taught by Chu to increase the effectiveness of the original compound for treatment of prostate cancer. A skilled artisan will be imbued with a reasonable expectation of success in developing such a dosage form based on the state of the art at the time of invention in order to develop an effective therapeutic agent with prolonged half lives and better bioavailability.

Conclusion

Claims 1-2 and 7-10 are rejected. No claims are allowed

Claims 3-6 and 11-14 are withdrawn as being drawn towards a non elected invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 8 am to 5 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614